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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/919,835	08/02/2001	Brigitte Bathe	211710US0X	4334

22850 7590 12/17/2004

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EXAMINER
FRONDA, CHRISTIAN L

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 12/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/919,835	BATHE ET AL.	
	Examiner	Art Unit	
	Christian L Fronda	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-60* is/are pending in the application.

4a) Of the above claim(s) *11-37* is/are withdrawn from consideration.

5)☒ Claim(s) *56 and 57* is/are allowed.

6)☒ Claim(s) *38-42,44,46-55 and 58-60* is/are rejected.

7)☒ Claim(s) *43 and 45* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/01,09/02,07/03,08/04*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission filed on 09/20/2004 has been entered.

2. Newly submitted claims 11-37 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

Claims 11-34 is directed toward a process for the fermentative preparation of an L-amino acid which is related to claims 38-60 as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product of claims 38-60 (isolated polynucleotides, vectors, host cells) can be used in a materially different process of using that product such as use in a recombinant process to make a polypeptide.

Claims 35 and 36 is drawn to a feedstuffs additive and is unrelated to the product of claims 38-60 since they are different products that have different classifications and require different searches.

Claim 37 is drawn to a process for obtaining RNA, cDNA and DNA to isolated nucleic acids, polynucleotides, or genes which encode a polypeptide having homocysteine methyltransferase I activity and is related to the product of claims 38-60 as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product of claims 38-60 (isolated polynucleotides, vectors, host cells) can be used in a materially different process of using that product such as use in a recombinant process to make a polypeptide.

A search of all claims 11- 60 in the patent literature and the non-patent literature cannot be made without serious burden because the inventions require separate searches that have different limits, boundaries, scope, and subject matter. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their divergent subject matter and classification, restriction for examination purposes is proper.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 11-37 are withdrawn from consideration as being directed to

a non-elected inventions. See 37 CFR 1.142(b) and MPEP § 821.03.

3. Applicants request filed 07/20/2004 that nonelected process claims which depend from or include all the limitations of an allowable product claim be rejoined and allowed is acknowledged.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

4. Claims 38-60 are under consideration in this Office Action.

5. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

6. The paper copy and computer readable form (CRF) of the Sequence Listing filed on 11/20/2001 have been received and have been processed by the Scientific and Technical Information Center (STIC).

7. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: an isolated polynucleotide from Corynebacterium encoding a homocysteine methyltransferase.

Claim Rejections - 35 U.S.C. § 112, 2nd Paragraph

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 40-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 40 is vague and indefinite because it is not clear if the recited "fragment thereof" refers to the polynucleotide that is 95% identical to SEQ ID NO:1 or the polynucleotide of claim 38, and because the particular function of the recited "fragment thereof" is not known and not recited.

For examination purposes, claim 40 is assumed to recite a fragment of a polynucleotide that is 95% identical to SEQ ID NO:1, where the fragment is not limited to any biological function.

Claim 41 is vague and indefinite because it is not clear if the recited "fragment thereof" refers to the polynucleotide that is 99% identical to SEQ ID NO:1 or the polynucleotide of claim 38, and because the particular function of the recited "fragment thereof" is not known and not recited.

For examination purposes, claim 41 is assumed to recite a fragment of a polynucleotide that is 99% identical to SEQ ID NO:1, where the fragment is not limited to any biological function.

Claim 42 is vague and indefinite because it is not clear if the recited "fragment thereof" refers to the polynucleotide of SEQ ID NO:1 or the polynucleotide of claim 38, and because the

particular function of the recited "fragment thereof" is not known and not recited.

For examination purposes, claim 42 is assumed to recite a fragment of a polynucleotide of SEQ ID NO:1, and where the fragment is not limited to any biological function.

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 40-42, 59, and 60 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 40 and 41 are a genus claims that is directed toward any fragment of any nucleotide sequence of a polynucleotide that is at least 95% and 99 % identical to SEQ ID NO:1, respectively. Claim 42 is a genus claim that is directed toward any fragment of the nucleotide sequence of SEQ ID NO: 1.

The scope of the each of the claims includes many polynucleotides with widely differing structural, chemical, and physical characteristics and widely differing biological functions. Furthermore, the genus is highly variable because a significant number of structural differences between genus members is permitted and genus members have different biological functions.

The specification discloses an isolated polynucleotide consisting of the nucleotide sequence of SEQ ID NO: 1 encoding a polypeptide consisting of the amino acid sequence of SEQ ID NO: 2. However, neither the specification nor the general knowledge of those skilled in the art provide evidence of any description of a structure and biological function which would be expected to be common to the members of the genus and would distinguish members of the genus from other polynucleotides. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed.

The disclosed polynucleotide of SEQ ID NO: 1 encoding the polypeptide of SEQ ID NO: 2 is not representative of the claimed genus since other members of the genus have widely differing nucleotide sequences, structures, and biological functions. The specification fails to provide a written description of representative polynucleotides encoding polypeptides as

encompassed by the claimed genus. Furthermore, there is no recitation of any particular structure to function/activity relationship in claims 40-42 that clarify what common biological function is shared by members of the claimed genus.

Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosed polynucleotide of SEQ ID NO: 1 encoding the polypeptide of SEQ ID NO: 2 alone is insufficient to describe the genus. In view of the above considerations, one of skill in the art would conclude that Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the invention of claims 40-42.

Amending each of claims 40-42 to recite that the fragment encodes a polypeptide that has homoscyteine methyltransferase I activity may overcome the rejection.

Applicants' arguments filed 07/20/2004, have been fully considered but they are not persuasive. Applicant's position is that the current amendment overcomes the written description rejection for claims 59 and 60. The Examiner respectfully disagrees for reasons of record as supplemented below.

Claims 59 and 60 are genus claims that are directed toward any isolated polynucleotide of any nucleotide sequence and biological function consisting of at least 15 consecutive nucleotides of SEQ ID NO: 1 or the full complement of SEQ ID NO: 1. The scope of the each of the claims includes many polynucleotides with widely differing structural, chemical, and physical characteristics and widely differing biological functions. Furthermore, the genus is highly variable because a significant number of structural differences between genus members is permitted and genus members have different biological functions.

SEQ ID NO: 1 is disclosed as consisting of 2810 nucleotides. However, neither the specification nor the general knowledge of those skilled in the art provide evidence of any description of a biological function or property which would be expected to be common to the members of the genus and would distinguish members of the genus from other polynucleotides. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed.

There is no recitation of any particular structure to function/activity relationship in claims 59 and 60 that clarify what common biological function is shared by members of the claimed genus. While the specification states that such polynucleotides consisting of at least 15 consecutive nucleotides of SEQ ID NO: 1 or the full complement of SEQ ID NO: 1 are suitable as DNA hybridization probes or primers (see p. 4, lines 15-20), claims 59 and 60 as written do not recite that the claimed polynucleotides are DNA hybridization probes or primers.

Since the disclosure fails to describe the common biological function or property that

identify members of the genus and because the genus is highly variant, one of skill in the art would conclude that Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the invention of claims 59 and 60.

12. Claims 38-41, 44, 46-55, and 58-60 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:2, an isolated polynucleotide comprising SEQ ID NO: 1, a fragment of the polynucleotide of SEQ ID NO: 1 encoding a homocysteine methyltransferase I, and a polynucleotide that encodes a polypeptide comprising a fragment of SEQ ID NO: 2 having homocysteine methyltransferase I activity; does not reasonably provide enablement for any other embodiment. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of claims 38-41 and 44 encompass any isolated polynucleotide that is at least 90%, 95%, or 99% identical to SEQ ID NO: 1 or any isolated polynucleotide encoding any polypeptide having homocysteine methyltransferase I activity and an amino acid sequence that is at least 90% identical to SEQ ID NO: 2.

The polynucleotide of SEQ ID NO: 1 is disclosed by specification as consisting of 2810 nucleotides which encodes a homocysteine methyltransferase I with amino acid sequence of SEQ ID NO: 2 consisting of 745 amino acids. Thus, claims 38 and 39 encompass polynucleotides that have 2529 nucleotides that are identical to SEQ ID NO: 1 and 281 nucleotides that are different (substitutions, deletions, or insertions with any nucleotide) from SEQ ID NO: 1 since the claim recites the limitation of 90% identity to SEQ ID NO: 1. Similarly, claim 40 which recites 95% identity to SEQ ID NO: 1 encompasses polynucleotides that have 2670 nucleotides that are identical to SEQ ID NO: 1 and 140 nucleotides that are different from SEQ ID NO: 1; and claim 41 which recites 99%identity to SEQ ID NO: 1 encompasses polynucleotides that have 2782 nucleotides that are identical to SEQ ID NO: 1 and 28 nucleotides that are different from SEQ ID NO: 1. Claims 38 and 44 encompass polynucleotides encoding polypeptides with amino acid sequences that have 671 amino acid residues that are identical to SEQ ID NO: 2 and 74 amino acid residues that are different (substitutions, deletions, or insertions with any amino acid

residue) from SEQ ID NO: 2 since the claim recites the limitation of 90% identity to SEQ ID NO: 2.

In order to meet the enablement requirement, one skilled in the art must be able to make the invention of claims 38-41 and 44 without undue experimentation using the specification coupled with information known in the art. However, neither the specification nor the general knowledge of those skilled in the art provide guidance or prediction on making, without undue experimentation, any isolated polynucleotide that is at least 90%, 95%, or 99% identical to SEQ ID NO: 1 or any isolated polynucleotide encoding any polypeptide having homocysteine methyltransferase I activity and an amino acid sequence that is at least 90% identical to SEQ ID NO: 2.

The specification does not provide guidance or prediction regarding the specific structural and catalytic amino acids residues in SEQ ID NO: 2 that are essential for enzyme activity which cannot be altered. Nor does the specification provide guidance or prediction regarding the specific amino acid residues within the full length polypeptide of SEQ ID NO: 2 that can be changed without destabilizing protein structure and inactivating enzyme activity. Furthermore, the specification does not provide working examples for selecting and changing the specific nucleotides in SEQ ID NO: 1 or amino acids in SEQ ID NO: 2 which does not affect homocysteine methyltransferase I activity and yet meet the claim limitations.

The general knowledge of those skilled in the art does not provide any guidance or prediction regarding the specific structural and catalytic amino acids residues in SEQ ID NO: 2 which cannot be altered, and specific amino acid residues in SEQ ID NO: 2 that can be changed without destabilizing protein structure and inactivating enzyme activity. The prior art as exemplified by Broun et al. (Science. 1998 Nov 13;282(5392):1315-7) teach that minor modifications to a protein sequence can completely alter the function of a protein. Broun et al. show that as few as four amino acid substitutions in a polypeptide consisting of 380 amino acid residues changes the enzymatic activity of the polypeptide from a desaturase to a hydroxylase (seen entire publication, especially the abstract and pp. 1316-1317).

Since neither the specification nor information known in the art provide guidance or prediction for the nucleotides in SEQ ID NO: 1 or amino acids in SEQ ID NO: 2 that can be changed without inactivating enzyme activity, one must perform an enormous amount of trial and error experimentation to determine which nucleotides in SEQ ID NO: 1 and amino acids in SEQ ID NO: 2 to change without inactivating homocysteine methyltransferase I activity.

Such trial and error experimentation is well outside the realm of routine experimentation and entails selecting any 281, 140, or 28 nucleotides in SEQ ID NO: 1 to modify, searching and screening for the type of modification to perform on the selected nucleotides (deletion, insertion, substitution, additions or combinations thereof) which will not result in a loss of enzyme activity and meet the claim limitations of 90%, 95%, or 99% identity to SEQ ID NO: 1, and expressing and assaying the polypeptide encoded by the modified polynucleotide to determine whether the

polypeptide has homocysteine methyltransferase I activity. Alternatively, such trial and error experimentation entails selecting any 74 amino acid residues in SEQ ID NO: 2 to modify, searching and screening for the type of modification to perform on the selected amino acid residues (deletion, insertion, substitution, additions or combinations thereof) which will not result in a loss of enzyme activity, determining whether the modified polypeptide has any homocysteine methyltransferase I activity, and then making the corresponding polynucleotide that encode the modified polypeptide. Teaching regarding screening and searching for the claimed invention using assays stated in the specification is not guidance for making the claimed invention.

The Examiner finds that one skilled in the art would require additional guidance, such as information regarding the amino acid residues in SEQ ID NO: 2 which can be changed without inactivating homocysteine methyltransferase I activity. Without such a guidance, the amount of experimentation left to those skilled in the art to make the claimed invention is undue and well outside of routine experimentation.

Claims 46-55 and 58 which depend from claim 38 are also rejected because they do not correct the defect of any claims 38.

The nature and breadth of the claims 59 and 60 encompass oligonucleotide probes that consist of at least 15 consecutive nucleotides of SEQ ID NO: 1 or consist of at least 15 consecutive nucleotides of the full complement of SEQ ID NO: 1.

The state of the prior art as exemplified by Sambrook et al. ('Types and uses of oligonucleotide probes'. In: Molecular Cloning A laboratory manual, 1989 second edition, pp. 11.3-11.10.) and Wallace et al. (Oligonucleotide Probes for the screening of recombinant DNA libraries. Methods Enzymol. 1987, Vol. 152, pp.432-443.) is such that determining the specificity of hybridization probes is empirical by nature and the effect of mismatches within an oligonucleotide probe is unpredictable. Even if the probe is a 20mer, the total number of hits in a database search is 143,797,728 which suggests that some of the probes encompassed by the claims would not preferentially hybridize to the nucleotide sequence of SEQ ID NO: 1. Therefore, it cannot be predicted which 15mer oligonucleotide probe will hybridize specifically and preferentially to the nucleotide sequence of SEQ ID NO: 1.

The specification does not provide guidance with respect to the specific nucleotide sequence of any oligonucleotide probe that consists of at least 15 consecutive nucleotides of SEQ ID NO: 1 or a full complement of SEQ ID NO: 1 that will specifically and preferentially hybridize to the nucleotide sequence of SEQ ID NO: 1. The amount of experimentation to determine the specific nucleotide sequence of any of the said oligonucleotide probes that will specifically and preferentially hybridize to the nucleotide sequence of SEQ ID NO: 1 is enormous. Such experimentation entails performing extensive hybridization experiments with every 15mer oligonucleotide probe possible to determine which 15mer oligonucleotide probe

will specifically and preferentially hybridize to the nucleotide sequence of SEQ ID NO: 1.

The Examiner finds that one skilled in the art would require additional guidance, such as information regarding the specific nucleotide sequence of the oligonucleotide probe which will specifically and preferentially hybridize to the nucleotide sequence of SEQ ID NO: 1 in a nucleic acid sample. Without such a guidance, the experimentation left to those skilled in the art is undue.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

14. Claims 38, 40-42, 44, 46-55, and 58-60 are rejected under 35 U.S.C. 102(e) as being anticipated by Pompejus et al. (US 2003/0049804 A1, published March 13, 2003).

Pompejus et al. teach the following:

(1) isolated nucleic acids, designated as MP (metabolic pathway) nucleic acid molecules encoding MP proteins, including an isolated polynucleotide (Identification code RXN02085, SEQ ID NO: 103) which encodes a polypeptide that has 99.89% identity to SEQ ID NO:2, where positions 10-2335 of RXN02085 encode the said polypeptide that has 99.89% identity to SEQ ID NO:2 (see enclosed alignment of RXN02085 to SEQ ID NO: 2).

Table 1, page 3, of US 2003/0049804 A1 shows that RXN02085 encodes an S-methyltetmhydropteroyltriglutamate-homocysteine methyltransferase (EC 2.1.1.14), which is also known in the prior art as homocysteine methyltransferase I (EC 2.1.1.14). RXN02085 which consists of 2358 nucleotides comprises a polynucleotide (positions 10-2335) which encodes homocysteine methyltransferase I having an amino acid sequence that is 99.89% identical to SEQ ID NO: 2; and thus, anticipate the invention of claims 38 and 44. Furthermore, since DNA exists as two strands, sense and antisense, then the disclosure of RXN02085 is also a

disclosure of the full complement of RXN02085, and thus anticipates claim 58.

(2) RXN02085 is a polynucleotide of 2358 nucleotides which has 100% identity to a fragment of SEQ ID NO: 1 at positions 217-2574, and as stated above encodes a homocysteine methyltransferase I (see enclosed alignment of RXN02085 to SEQ ID NO:1). Thus, this teaching anticipate the invention of claims 38 and 40-42,which recite a fragment of SEQ ID NO: 1.

(3) the isolated MP nucleic acid molecules, including the isolated polynucleotide RXN02085 stated above, are isolated nucleic acid molecules of cDNAs, DNAs, or RNAs (see p. 2, paragraph **[0012]**, lines 1-2). Thus, this teaching anticipate the invention of claim 46.

(4) vectors that are capable of replication in coryneform bacterium that comprise the isolated MP nucleic acid molecules, including the isolated polynucleotide RXN02085 stated above, where the said vectors contain regulatory sequences including promoters, repressor binding sites, and enhancers (see p. 15, paragraphs **[0092]** to **[0095]**; and EXAMPLES 5-10). Thus, these teachings anticipate the invention of claims 47-49.

(5) host cells that comprise vectors comprising the isolated polynucleotide RXN02085 stated above, where said polynucleotide RXN02085 is present on a plasmid (see p. 15, paragraph **[0093]**). Thus, these teachings anticipate the invention of claims 50 and 52. Because the said vectors replicate in host cells, then the host cell will have more than one copy of the said polynucleotide RXN02085, and thus anticipate claim 51.

(6) host cell where the isolated polynucleotide RXN02085 stated above is integrated into the genome of the host cell (see p. 4, paragraph **[0026]**, lines 7-8). Thus, the teaching anticipates the invention of claim 53.

(7) host cell comprising the isolated polynucleotide RXN02085 stated above which can be expressed in bacterial cells such as *Corynebacterium glutamicum*. Thus, the teaching anticipates the invention of claims 54 and 55.

(8) fragments of the isolated polynucleotide RXN02085 serving as oligonucleotide primers or probes, where the oligonucleotide is preferably about 25, 40, 50, 70 consecutive nucleotides of the sense or antisense strand of the polynucleotide RXN02085 (see pp.9-10, paragraph **[0070]**). Since RXN02085 is a polynucleotide of 2358 nucleotides which has 100% identity to a fragment of SEQ ID NO: 1 at positions 217-2574 , then this 2358 nucleotide fragment falls within the scope of "at least 15 consecutive nucleotides of SEQ ID NO: 1".

Thus, these teaching anticipates claim 59, which recite polynucleotides consisting of at

least 15 consecutive nucleotides of SEQ ID NO:1. Furthermore, since DNA exists as two strands, sense and antisense, then the disclosure of RXN02085 is also a disclosure of the full complement of RXN02085, and thus anticipates claim 60, which recites "at least 15 consecutive nucleotides of the full complement of SEQ ID NO: 1".

US 2003/0049804 A1 claims priority to US Provisional Application No. 60/148,613, filed 08/12/1999, and is considered prior art, as defined by 35 U.S.C. 102(e), because US Provisional Application No. 60/60/148,613 discloses and has support for the isolated polynucleotide RXN02085 (SEQ ID NO: 103), vectors, and host cells stated above. The nucleotide sequence of polynucleotide RXN02085 is shown on Appendix A, pages 157-158, and the encoded amino acid sequence is shown on Appendix B, page 50, of US Provisional Application No. 60/148,613.

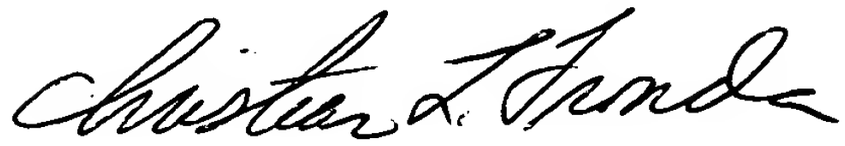
Conclusion

15. Claims 56 and 57 are allowed.

16. Claims 43 and 45 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

18. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Christian L. Fronda
Patent Examiner
Art Unit 1652